Female Alopecia in Prospective Mothers as a More Specific Risk-Factor for Down's Syndrome and Other Genetic Abnormalities than Age Alone

17 December 2022
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Introduction

As shown in this graph, the spike in the risk of Down's Syndrome associated with the age of the mother increases nearly exponentially starting at, according to our best data, at about age 38. The current medical doctrine on this topic states that the chronological age of a woman's eggs leads to the degradation of the DNA contained therein, thereby increasing the risk of anomaly in the fetal development process.

Abstract

I would suggest that the sharp increase in risk at age 38 is actually inconsistent with a gradual and uniform genetic degradation in oocyte DNA and is more consistent, given that Trisome 21 is, by a wide margin, the most common genetic anomaly in children of mothers who give birth at over age 40, with a disorder of mRNA homeostasis that starts not at conception, but rather, in third through fifth week of fetal development, after the umbilical cord joins with the placenta.

It is no coincidence that another common medical issue affecting women sets in, on the average, at the exact same age as the age at which Trisome 21 becomes a reproductive issue... hair loss. The rate at which younger women suffer alopecia and the rate at which younger women give birth to Down's Syndrome babies is nearly identical, as are the rates at which women over a certain age fail to contract alopecia and the rate of uncomplicated pregnancy in older women.

This correlation caused my attention to be drawn to a hormone called Follicle-Stimulating Hormone, which is a necessary growth factor needed to facilitate hair growth. FSH enables follicles of all sorts (not only hair follicles) to make copies of proteins. In the absence of this hormone, follicles can shut down entirely and the protein production process not only stops, but proteins already manufactured detach from the follicle. While hair loss is a merely cosmetic issue, the hormonal deficiency that underlies it has wider health implications. For the function of the placenta, this may mean decreased efficiency of the exchange of materials between the mother's and fetus' blood. Included in these materials are things like oxygen, carbon dioxide, glucose, plasma, and messenger RNA.

In order for the placental barrier to perform its task of exchanging nourishment and waste, materials must be transported between the portion of the placenta composed of the mother's blood vessels (mother's DNA) and the others, made of blood vessels derived from fetal DNA. These two networks of blood vessels, although they are closely intertwined, are not meant to connect directly. In fact, direct bridging between mother's and baby's circulatory

systems is fatal when blood types do not match.

Rather than direct bridging, exchange of nourishment and waste is achieved with the help of proteins, which have to be secreted by follicles on the outside of the mother's blood vessels in the placenta, extending like an air lock between two spacecraft toward the fetal blood vessels. The proteins act as a conductive medium passing through a semi-permeable membrane, allowing the conduction of only certain elements of mother's and baby's blood through the barrier. While the meeting of fetal and maternal placenta is, in most respects, a meeting at the halfway point, when it comes to these conductive proteins, they can only come from the mother.

If a mother lacks a sufficient quantity of FSH, these follicles, like hair follicles, will not create adequate bridges to support the exchange of materials, increasing the risk of miscarriage, stillbirth, and in particular, Trisome 21. What is so special about Trisome 21 that it correlates so strongly with a woman's age? If this hypothesis proves correct, what causes mRNA disequilibrium brought on by reduced efficiency of homeostatic processes to lead to Trisome 21 more than any other mutation?

When a fetus is in the zygotic stage, prior to umbilical cord formation, it is made of a sufficiently small number of cells that cellular messaging can proceed nominally without the aid of a cellular interstitia. At this stage, a fetus does not have its own interstitia; a newly discovered organ system responsible for carrying mRNA signals throughout the body outside of the circulatory system. This system works best in an adult who keeps active and is not exposed to zero-gravity environments. The interstitia, as I wrote about in a previous publication, depends upon both osmosis and reverse osmosis. Fluids and their contents settle and collect in certain areas when we are sedentary and thus, sedentary behavior leads to genes needing to overexpress themselves to deliver signals reliably. This can lead to a cascade of cellular dysfunction which shortens life-expectancy and increases the risk of cancer.

A fetus at about week 3-5 of development, being that it depends largely upon its mother's circulatory system for nearly everything, absent its own interstitia, depends upon an efficiently functioning placental barrier for mRNA homeostasis.

What sorts of mRNA signals is a 3-5 week fetus sending from one end of its body to the other, predominantly? I would suggest that instructions to divide are the most common, given the phenomenal rate of growth at this stage. Every cell in such a fetus is going to nearly constantly say, if only chemically, to its neighboring cells, "I am ready to divide, are you?" to which the other cells respond, ideally, "Yes." in a prompt manner. A delay in response or a failure to reply could result in deformities that result in asymmetrical growth. Symmetry of growth is determined almost exclusively by the efficiency with which mRNA homeostasis is maintained.

If "divide" instructions accumulate as a result of a failure of the placental barrier's natural mechanism, nearly all of the many thousands of cells in the fetus could gradually convert to a state of Trisome 21. Trisome 21 results from the division of the 21st chromosome into a third segment. This may result

from an abundance of improper signals telling a cell, beginning with its DNA, to duplicate itself in the face of other, contradictory signals. With Trisome 21, a molecule meant to simply "cut" (perhaps CAS9) a duplicate chromosome meant to form the heart of a new cell winds up mistakenly dividing the only available copy of the DNA into the characteristic third segment. This may be the result of a process of signals and counter-signals that allow for some processes to be halted midway through (the instruction to copy, for instance) but not the other, related process for cutting that duplicated DNA. A metaphor for this would be if the President ordered a coordinated bomber and cruise missile strike and then changed his mind. While the bombers can be recalled, the cruise missiles (let's say they are the older cruise missiles that can't be reprogrammed) are locked into a course of action and do considerable damage despite a desire to recall them.

This is quite distinct from the current doctrine that holds that Down's Syndrome is set from the moment of insemination of the egg and the setting of the original genetic code of the fetus. Although counter-intuitive, this hypothesis has a high degree of plausibility given that we already know that although sex is determined at conception, mutations such as hermaphrodism can set in as late as the 6th week of fetal development.

If the sex of a portion of a fetus can be altered after conception due to mutation, then it stands to reason that not all genetic abnormalities are bestowed at conception. Some, namely Down's Syndrome, may come about closer to week 4 when the function of a mother's placental barrier becomes critical.

Conclusion

Although restoring the function of placental barrier protein follicles in cases where they have already been deactivated would likely be more involved a process than merely prescribing an FSH supplement, the evaluation of FSH levels may provide a useful data point to prospective mothers to guide their reproductive decisions. FSH levels may be the deciding factor in identifying the rare few who, despite being young, should eschew reproduction and those who, despite being older, should not discount it.